PTPN12 gene expression signature in triple negative breast cancer cohort

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Methods

105 gene expression array analysis of triple negative breast cancer patients (TN). The effects of PTPN12 appear to be mediated through several known tyrosine receptors including EGFR and Her2. We investigated the effects of PTPN12 gene expression variation, gene expression data obtained from 105 TN patients using this approach. In order to gain further insight into the molecular mechanism of PTPN12 and its relevance to TN breast cancer, we performed gene expression analysis of the 105 TN patients. We identified seven distinct gene clusters and three distinct patient subpopulations. The three distinct subgroups of TN patients were comprised of low expressing TNs (P1), medium expressing TNs (P2), and high expressing TNs (P3). The first two subpopulations were formed by PTPN12 mRNA levels, and the third one was determined by IHC (for ER, PR, and Her2) and by FISH (for Her2). Gene expression analysis of the 105 TN patients was performed using Illumina HT-12 platform which contains over twenty thousand probes. We performed the analysis on a genome-wide scale using the Illumina gene expression data we received from the two subpopulations. The first two subpopulations were formed by PTPN12 mRNA levels, and the third one was determined by IHC (for ER, PR, and Her2) and by FISH (for Her2). Gene expression analysis of the 105 TN patients was performed using Illumina HT-12 platform which contains over twenty thousand probes. We performed the analysis on a genome-wide scale using the Illumina gene expression data we received from the two subpopulations.

Results

Distribution of PTPN12 mRNA Levels in 105 Triple Negative Breast Cancer Patients

Figure 1 – Distribution of PTPN12 mRNA expression levels in 105 breast cancer patients.

We then performed two-dimensional hierarchical clustering of the 1000 top correlated genes with PTPN12 expression across the 105 TN samples. We identified seven distinct gene clusters and three distinct patient subpopulations. The three distinct subgroups of TN patients were comprised of low expressing TNs (P1), medium expressing TNs (P2), and high expressing TNs (P3). Upon examining the genes within each cluster, we found that all contain unique sets of genes belonging to the EGFR and FGF signaling pathways, and 6 genes involved in mitosis. It is worth noting that EGFR expression of PTPN12 (P3) was significantly higher in high PTPN12 expressing patients. We performed two-dimensional hierarchical clustering of the 1000 top correlated genes with PTPN12 expression across the 105 TN patients. We also performed comprehensive pathway analysis using the DAVID bioinformatics tool on the genes as input to the GSEA software (2.0). All the gene expression analyses were performed using R software (version 2.15.3).

Conclusion

PTPN12 tyrosine phosphatase may play an important role in tumor development/progression in triple negative breast cancer patients (TN). The effects of PTPN12 appear to be mediated through several known tyrosine receptors including EGFR and Her2. We investigated the effects of PTPN12 gene expression variation, gene expression data obtained from 105 TN patients using this approach. In order to gain further insight into the molecular mechanism of PTPN12 and its relevance to TN breast cancer, we performed gene expression analysis of the 105 TN patients. We identified seven distinct gene clusters and three distinct patient subpopulations. The three distinct subgroups of TN patients were comprised of low expressing TNs (P1), medium expressing TNs (P2), and high expressing TNs (P3). Upon examining the genes within each cluster, we found that all contain unique sets of genes belonging to the EGFR and FGF signaling pathways, and 6 genes involved in mitosis. It is worth noting that EGFR expression of PTPN12 (P3) was significantly higher in high PTPN12 expressing patients. We performed two-dimensional hierarchical clustering of the 1000 top correlated genes with PTPN12 expression across the 105 TN patients. We also performed comprehensive pathway analysis using the DAVID bioinformatics tool on the genes as input to the GSEA software (2.0). All the gene expression analyses were performed using R software (version 2.15.3).

Figure 1 – Distribution of PTPN12 mRNA expression levels in 105 breast cancer patients.

Figure 2 – Two-dimensional hierarchical clustering of the 1000 top correlated genes with PTPN12 mRNA expression across the 105 TN samples. The three distinct patient clusters are denoted by P1 (gray), P2 (red), and P3 (green) and the seven distinct gene clusters are denoted by C1 through C7.